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## Ileus and Ignorance

WITH THE INTRODUCTION OF general anesthesia, antisepsis, and later asepsis, the success of the treatment of intra-abdominal disease by operation increased dramatically. This remarkable achievement was tempered by the recognition that mechanical manipulation of the bowel was accompanied by a temporary paresis of bowel activity that typically lasted from five to seven days. Early in this century, bowel dysfunction after an operation was life-threatening as oral intake was accompanied for several days by intractable vomiting, distention, aspiration, cardiac arrhythmia, and even death from "acute gastric dilatation." In the absence of sterile solutions for intravenous replacement, surgeons resorted to cumbersome infusions into the rectum and subcutaneous tissues ("clysis") to avoid profound dehydration. This digestive derangement was called "paralytic" or "adynamic" ileus to emphasize its transitory and functional nature and to distinguish it from time-honored mechanical ileus or dynamic intestinal obstruction. Despite countless explanations and remedies proposed over the past 100 years, the problem of postoperative ileus remains largely unresolved. Now, in this issue of the journal, Disbrow and co-workers propose the bold new idea that carefully directed preoperative suggestion has the power to hasten the return of bowel function after an operation.<sup>1</sup>

Aboral propulsion of liquid, gas, and chyme is the result of highly integrated activity of the stomach, small intestine, and colon. Parasympathetic nerves stimulate bowel contraction and relax enteric sphincters, thereby facilitating propulsion, whereas sympathetic nerve stimulation inhibits bowel activity and promotes ileus. Because many of the signs and symptoms of postoperative ileus—meteorism, hypoactive bowel sounds, anorexia, vomiting, and lack of flatus with exacerbation by eating and drinking—resemble those seen with acute nonabdominal conditions such as meningitis, pneumonia, and fractures, primary causation has long been attributed to "stress" or sympathetic-catecholamine overactivity.

A major step in understanding the pathogenesis of ileus was made when Wangenstein showed by careful studies in animals and patients that the bulk of intestinal gas arises from the swallowing of air and that symptomatic relief of acute ileus can be achieved by inserting a flexible tube into the stomach, causing immediate gastric decompression.<sup>2</sup> The recovery of bowel activity is spontaneous but variable, with the small intestine evincing segmental contractions even during an operation and coordinated peristalsis restored four to six hours after wound closure. In contrast, gastric paresis typically lasts

two to three days, right colon inertia three to four days, and dysfunction of the entire colon as long as five to six days before gas traverses the full length of the digestive tract. With the recognition that cardiac rhythm is regulated by myoelectric wave conductance through the sinoatrial and atrioventricular nodes to the ventricular chambers, an analogous concept gradually evolved to invoke an intrinsic gastrointestinal pacemaker for the control of peristalsis.<sup>3</sup>

Based on these limited insights, many innovative therapies have been advocated to accelerate the return of peristalsis after a laparotomy. Parasympathomimetics such as bethanechol chloride and neostigmine (an anticholinesterase), ganglionic blockers such as guanethidine, smooth muscle stimulants such as pilocarpine, cholecystokinin, motilin, and ceruletide (caerulein),  $\alpha$ -adrenergic antagonists such as chlorpromazine and phentolamine,  $\beta$ -adrenergic blockers such as propranolol, dopamine antagonists such as metoclopramide, and vasomediators such as vasopressin, prostaglandins, and dihydroergotamine were each introduced and championed for decades but eventually found wanting. Other remedies have included the administration of supplemental oxygen and even pressurized (hyperbaric) oxygen to wash out slowly diffusible intraluminal nitrogen, spinal anesthesia to block preganglionic sympathetics, pantothenic acid (a necessary substrate for coenzyme A and the synthesis of acetylcholine), hypertonic saline solution, whole blood transfusions, hot packs on the abdomen, and even operations such as adrenalectomy, ileocelectomy, or multiple "blow-hole" enterostomies. Again, after initial enthusiasm, these "panaceas" were eventually abandoned. The insertion of pacing electrodes for the direct stimulation of bowel contraction has also had disappointing results, as has transabdominal cutaneous nerve stimulation, a technique more akin to acupuncture than to western physiologic science. The discovery of enkephalins (opiate receptors) in the intrinsic nerve plexus of the bowel wall has encouraged the administration of antinarcotics such as naloxone to treat postoperative ileus.<sup>4</sup> Whereas the (ab)use of morphine, heroin, and other natural and synthetic narcotics is often responsible for severe constipation and obstipation, the use of opiate antagonists for the treatment of adynamic ileus remains unconvincing. Some data support the efficacy of an indwelling nasogastric balloon tube with "suction busting holes" to evacuate all swallowed air and thereby relieve bowel distention; a standard nasogastric tube is notoriously inefficient for this purpose and actually aggravates the swallowing of air. Whereas this specially designed balloon tube permits early postoperative feeding, its routine use has not gained widespread acceptance for simple procedures such as appendectomy and cholecystectomy and is potentially risky for complex operations involving bowel resection and a fresh anastomosis, such as gastrectomy and colectomy. Despite studies documenting that postoperative ileus is largely independent of the duration of the operation or of anesthesia or the degree of bowel manipulation, minimally invasive operations such as lap-

aroscopic cholecystectomy or fallopian tubal ligation and simple appendectomy are rarely accompanied by impaired gastrointestinal function, and oral intake is generally well tolerated within 24 hours of the procedure.

In this setting of hypothetic neurogenic, metabolic, pharmacologic, and inflammatory mediators in the pathogenesis of postoperative ileus but with general ineffectiveness of available treatment, Disbrow and colleagues examine the concept that increasing patients' awareness of impending bowel dysfunction preoperatively might shorten its duration postoperatively.<sup>1</sup> In a carefully designed prospective protocol, they establish reasonable criteria to monitor the development of ileus and to compare the time of the return of bowel function in two demographically comparable patient groups. One subgroup (control) received standard verbal reassurance regarding the impending operation, and the other (experimental) received specific "instructions" regarding the upcoming bowel dysmotility and the desirability of oral intake as soon as possible after the operation.

At first blush, the efficacy of such psychological reinforcement seems counterintuitive because conventional wisdom teaches that autonomic function is involuntary and independent of conscious thought. Yet, as Disbrow and associates point out, several clinical and experimental studies support the notion that the digestive tract is receptive to "learning," either by direct brain stimulation as in rats or through skinnerian operant conditioning in patients with intractable vomiting, fecal incontinence, or esophageal motility disorder. Perhaps an even more telling example of the influence of thought processes on autonomic function is peptic ulcer disease. Although recent evidence implicates bacterium (*Helicobacter pylori*) in the genesis of stomach ulcers, almost 175 years ago Beaumont described hyperemia of the stomach and the outpouring of gastric juice when Alexis St Martin, a young man with a permanent gaping, prolapsed gastric fistula as a result of a shotgun wound, became angry and upset.<sup>5</sup> A modern version of near-identical gastroautonomic responses to anger and hostility was reported in the case of "Tom," a victim of childhood corrosive gastritis and a well-developed, herniated, redundant gastric stoma.<sup>6</sup> Recognizing the role of psychic factors in the development of gastric and duodenal ulcers, Dragstedt extended the observations of Pavlov and documented the hypersecretion of acid-rich gastric juice between meals—for instance, at night—in patients with an ulcer diathesis and then showed that the interruption of vagal nerve bundles promoted ulcer healing.<sup>7</sup> In fact, until the widespread use of histamine ( $H_2$ ) and proton blockers, disconnection of the brain-autonomic axis—that is, transecting vagi—was a common way to treat intractable peptic ulcer. Other gastrointestinal disorders thought to be "consciously" mediated through the autonomic nervous system include spastic colitis and irritable bowel, disorders characterized by recurring vague abdominal pain and intermittent diarrhea in high-strung people. Long postulated, too, but far from proved is the emotional or psychosomatic component responsible for the disabling

inflammatory bowel diseases of regional ileitis and ulcerative colitis.

Other information also supports the influence of the psyche on autonomic dysfunction, with the relief of signs and symptoms by suggestion through biofeedback. Thus, with repetitive training, hand temperature, sweating, blood pressure, and even heart rate can be consciously self-regulated, and such learned behavior is used effectively to treat migraine, hypertension, and certain atrial arrhythmias and even to subvert the results of a polygraph or lie-detector test, a device that primarily depends on the interpretation of autonomic reactions—breathing, blood pressure, and the galvanic skin response.

Using blinded observers for ranking intraoperative bowel manipulations and assessing recovery variables from postoperative ileus, including time to first passage of flatus and length of hospital stay, Disbrow and associates found that instructed subjects (experimental) had a statistically shorter duration of ileus and earlier discharge than noninstructed but nonetheless reassured patients (control). There were also trends showing that instructed patients had a more rapid return of bowel sounds, faster removal of the nasogastric tube, and an earlier oral intake of liquids, with projected savings in hospital costs and, of course, less patient discomfort overall. Even though the ranking of operative criteria was carefully defined, it still would have been preferable to know exactly what operative procedures were done in the two groups. Moreover, with only 20 patients in each subgroup, a crossover of marginal data in as few as one or two patients may have negated the trends and statistical significance of the trial. Finally, past experience with "conscious activation" and autonomic (dys)function, such as in the development of peptic ulcer or biofeedback control of migraines, indicates that considerable time must transpire or conscious effort be expended—in other words, far greater mental activity than that afforded by a briefing just before an impending laparotomy.

Despite these criticisms and some skepticism, support for this study comes from findings after subliminal suggestive stimuli in patients operated on under general anesthesia. In these asleep patients, in contradistinction to awake subjects, specific ideas are verbally transmitted under full anesthesia. Although explicit memory—that is, free recall, cued recall, recognition, or free association—shows no retention, implicit memory or information processing is preserved by the performance of specific tasks by the patients after the operation in response to therapeutic suggestions transmitted under anesthesia.<sup>8</sup> Indeed, Cork and co-workers conclude, "[I]f this technique [intraoperative suggestion] could be further developed, perhaps common postoperative side-effects (e.g., nausea, emesis, difficulties with bowel and bladder function) could be minimized and pain management and overall outcome could be improved."<sup>8(p897)</sup> Whereas it is still premature to conclude that loud and coarse hard-rock or rap music subliminally seduces listeners into committing violent crimes, it is not overly far-fetched to consider that after a century of groping

ignorance and therapeutic paralysis, postoperative ileus may someday yield to simply putting in a few well-timed good words just before, during, and after an operation.

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